REMARKS

Claims 1, 3, 7-15, and 17-19 and 21-45 were pending in the application. Claims 10-14, 18, 21, and 23-45 have previously been withdrawn. Claims 2, 4-6, 16, 20 and 46-47 have previously been canceled. Claims 1, 3, 7-15, 17-19, 21, and 22-45 are thus pending, with claims 1, 3, 7-9, 15, 17, 19, and 22 under examination. No new matter has been added.

Rejection of Claims 1, 3 and 22 Under 35 U.S.C. § 102(e)

Claims 1, 3 and 22 stand rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Bonjouklian *et al.* (U.S. Patent No. 5,504,103). Specifically, the Examiner states that "Bonjouklian *et al*., teach methods of treating phsphatidylnositos-3-kinase [sic] dependent conditions in a mammal comprising contacting the cell with wortmannin or wortmannin analog" (page 4 of the Office Action). The Examiner more specifically states that "[t]ough [sic] Bonjouklian *et al*., does not specifically teach contacting T cells, T cells are abundantly present in mammals and inherently express phosphatidylinositol 3-kinase" (page 4 of the Office Action).

Applicant respectfully traverses the rejection. Applicant submits that Bonjouklian *et al.* teach methods of treating a certain number of phosphatidylinositol 3-kinase-dependent conditions using wortmannin *analogs*, such as 17β-hydroxywortmannin shown in formula I (col. 2), and *not* treating certain conditions using wortmannin itself (formula II, col. 3). Bonjouklian *et al*. describe that "[t]he compounds of formula I generally are known in the art, and are derived from wortmannin" (col. 2, lines 28-29). This is further evidenced by the claims of Bonjouklian *et al*. (col. 14-16, claims 1-20), which are directed to the use of a compound of formula I *only*.

The Examiner contends that "T cells are abundantly present in mammals and inherently express phosphatidylinositol 3-kinase. This finding is *supported by the applicant disclosure* in Figures 3, 4, 7a and 7b" (*emphasis added*, page 4 of the Office Action). The Examiner has incorrectly used hindsight reconstruction in formulating the rejection. The expression of phosphatidylinositol 3-kinase by T cells was not known at the time of Bonjouklian *et al*. Furthermore, the findings by Applicant in Figures 3, 4, 7a and 7b, showing that contacting $CD28^+$ T cells with wortmannin results in inhibition of phosphatidylinositol 3-kinase is novel. Also, Bonjouklian *et al*. lists diseases whose pathophysiology are T cell *independent*, such as

pain, diabetes, inflammation, platelet aggregation, vascular diseases, and various neoplasms (see col. 6, lines 6-18). Bonjouklian *et al.* does not teach or suggest the use of wortmannin for the treatment of any T cell-mediated disease processes. Moreover, Bonjouklian *et al.* does not teach or suggest a method to inhibit T cell activation or inhibit production of IL-2 by the T cell. In light of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Rejection of Claims 1, 3, 7, 15, 17, 19 and 22 Under 35 U.S.C. § 112, First Paragraph: Enablement

The Examiner has rejected claims 1, 3, 7, 15, 17, 19 and 22 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Specifically, the Examiner contends that the specification, "does not reasonably provide enablement for claims directed to a method of inducing unresponsiveness to an antigen in a T cell with the intended use of treating a human subject suffering from an autoimmune disease" (page 6 of the Office Action).

Applicant respectfully traverses the rejection. Based on the teachings of the instant specification, one of ordinary skill in the art could readily induce unresponsiveness to an antigen in a T cell. Applicant agrees with the Examiner's statement that "inflammatory and autoimmune disorders differ in etiologies and therapeutic endpoints" (page 8 of the Office Action), however, even though there are a number of etiologies and therapeutic endpoints to describe all autoimmune diseases, one of ordinary skill in the art would appreciate that it is desirable to downmodulate an immune response, i.e., to inhibit T cell activation in a subject suffering from any autoimmune disorder.

The Examiner also states, "[t]he quantity of experimentation required to practice the methods as claimed would require the de novo determination of effective target sites, modes of delivery, safe administration of an agent that inhibits PI3K and formulations of the claimed agent" (page 9 of the Office Action). Applicant submits that only routine experimentation would be needed to practice the invention as claimed. The alleged de novo determination of effective target sites would not be required, since the target site of the invention is the inhibition of T cell activation and production of IL-2 by the T cell. Effective modes of delivery and determination of safe administration of *any* pharmaceutical agent are routinely performed by one of ordinary

skill in the art. Further, based on the teachings of the instant application, for example, on page 8, lines 4-16, page 9, lines 14-31 and page 11, line 25 to page 12, line 7, one of ordinary skill would only need to perform routine experimentation to practice the invention. Reconsideration and withdrawal of this rejection is, therefore, respectfully requested.

Rejection of Claims 1, 3, 7-9 Under Nonstatutory Obviousness-Type Double Patenting

Claims 1, 3, and 7-9 stand rejected on the grounds of nonstatutory obviousness-type double patenting, as allegedly being unpatentable over claims 1-4 and 7-10 of U.S. Patent No. 6,632,789. Applicant respectfully requests that the Examiner hold all nonstatutory obviousness-type double patenting rejection in abeyance, until allowable subject matter is determined.

CONCLUSION

Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to **Deposit Account No. 06-1448, WYS-014.02**.

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Customer No.: 25181

Respectfully submitted,

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